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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,422	08/10/2001	Gary Van Nest	377882001420	6952

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,422	NEST ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) *24-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 48-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed April 8, 2004 is acknowledged and has been entered. Claims 48 and 70 have been amended. Claims 1-23 and 48-84 are now pending and being examined in the present application. All rejections have been withdrawn in view of Applicants' amendments and/or comments with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. This application contains claims 24-47 drawn to an invention nonelected with traverse in the reply filed on September 22, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

4. The Van Nest Declaration under 37 CFR 1.132 filed April 8, 2004 is sufficient to overcome the rejection of claims 1-21, 48-67, 70-78 and 81-84 based upon 112, first paragraph, enablement.

5. Claims 1-23 and 48-84 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15, 18-22, 27-29 and 51-62 of copending Application No. 10/214799. Although the conflicting claims are not identical, they are not patentably distinct from each

other because both applications claimed a complex comprising an IMP/MC, immunomodulatory polynucleotide (or oligonucleotide) and a microcarrier, covalently or non-covalently linked, as well as claims to a kit comprising said complex. The complex can also comprise an antigen. The microcarrier can be a liquid phase or solid phase microcarrier. The IMP can vary in length and can comprise a phosphate backbone modification.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

This rejection is maintained for the reasons of record.

6. Claims 13, 29-21, 60, 66, 67 and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims (claim 13 for example) lack positive antecedent basis in the recitation of "5'-TCGTCGX$_1$-3'"; this is not one of the sequences of claim 12.

Applicant's arguments filed April 8, 2004 have been fully considered but they are not persuasive. Applicants have asserted that claim 12 recites the sequence "5'-TCGX$_1$X$_2$X$_3$X$_4$-3'" "wherein X$_1$ X$_2$ X$_3$ X$_4$ are nucleotides." Claim 13 is directed to the claim 12 sequence where X$_1$X$_2$X$_3$ are TCG and the remaining X$_1$ is a nucleotide. However, the remaining or undefined X is X$_4$ not X$_1$, as set forth in the claims, since Applicants state that X$_1$X$_2$X$_3$ are TCG. There is no antecedent basis found in claim 12 for the sequence set forth in claim 13.

7. Claims 1-23 and 48-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Carson et al (WO 98/16247), Ray (WO 99/11275) or Schwartz et al (WO 98/55495).

The claims are directed to a IMP/MC complex that comprises a polynucleotide (sequence 5'-C, G-3', greater than 6 nucleotides) linked (non-covalently or covalently) to the surface of a microcarrier and may comprise an antigen (i.e. allergen). The MC is a liquid phase or solid phase or cationic and is less than 10 microns in size. The polynucleotide may be SEQ ID NO: 1 or have a phosphate backbone modification (phosphorothioate).

Schwartz et al, for example, discloses a complex that comprises an oligonucleotide in conjunction with an immunostimulatory peptide or antigen (abstract; p. 4). The prior art discloses that the complex can also comprise an encapsulating agent that can maintain the ISS and antigen (pp. 7-8; p. 13). Schwartz et al discloses that the oligonucleotides (i.e. ISS or IMP) comprise phosphorothioate backbones, which are phosphate backbone modifications (p. 11; p. 29). Schwartz et al discloses that the oligonucleotide can be combined with immunomodulatory facilitators such as adjuvants, such adjuvants include emulsions and polylactide/polyglycolide microparticles (i.e. MC) (p. 12, 14; claims). Schwartz et al discloses that the ISS can be covalently or non-covalently linked to the immunomodulatory facilitator (i.e. MC) (p. 14). The prior art discloses the nucleotide sequence as set forth in Applicants' SEQ ID NO: 1 (see SEQ ID NO: 15). It is noted that claims 48-84 are directed to a kit. The components of the kit are the same as the components of claims 1-23 and it would appear that Schwartz et al would disclose the claimed kit. Determining the size of the microparticle would have been within the knowledge of a skilled since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

Since the Patent Office does not have the facilities for examining and comparing applicants' complex and kit with the complex and kit of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed complex and kit and the complex and kit of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

The rejection of claims 1-23 and 48-84 under 35 U.S.C. § 102(b) as anticipated by Carson et al (WO 98/16247), Ray (WO 99/11275) or Schwartz et al (WO 98/55495) is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 1-23 and 48-84 under this statutory provision, as set forth in the last Office action. Applicants' arguments filed April 8, 2004, have been fully considered but they are not deemed to be persuasive.

Applicants have asserted that none of the references anticipate the claimed invention. Applicants have asserted that Schwartz describes co-administration of an immunostimulatory polynucleotide (ISS), antigen and adjuvant, where the adjuvant includes emulsions, alum, liposomes and microparticles. Schwartz also describes compositions comprising an ISS, an immunomodulatory molecule and an encapsulating agent in the form of emulsions, microparticles and/or liposomes and "adjuvant oil-in-water emulsions, microparticles and/or liposomes encapsulating an ISS-immunomodulatory molecule in the form of particles." Applicants further state that although Schwartz describes mixtures of ISS with antigen and adjuvant, including microcarriers, Schwartz does not describe a complex in which an IMP is linked to the surface of a microcarrier.

However, it is noted that Schwartz disclose that "the term conjugate refers to a complex in which an ISS and an immunomodulatory molecule are linked. Such conjugate linkages include covalent and/or non-covalent linkages." (p. 12). Schwartz disclose that the "ISS can be administered in conjunction with one or more immunomodulatory facilitator. Thus, the invention provides compositions comprising ISS and an immunomodulatory facilitator. As used herein, the term "immunomodulatory facilitator" refers to molecules, which support and/or enhance the immunomodulatory activity of an ISS. Examples of immunomodulatory facilitators can include co-stimulatory molecules, such as cytokines, and/or adjuvants. The ISS and facilitator can be administered as an ISS-facilitator conjugate and/or they can be co-administered as a complex in the form of an admixture, such as in an emulsion. The association of the ISS and the facilitator molecules in an ISS-facilitator conjugate can be through covalent interactions and/or through non-covalent interactions, including high affinity and/or low affinity interactions. Examples of non-covalent interactions that can couple an ISS and a facilitator in an ISS-facilitator conjugate include, but are not limited to, ionic bonds, hydrophobic interactions, hydrogen bonds and van der Waals attractions. Immunomodulatory facilitators include, but are not limited to, co-stimulatory molecules (such as cytokines, chemokines, targeting protein ligand, trans-activating factors, peptides, and peptides comprising a modified amino acid) and adjuvants (such as alum, lipid emulsions, and polylactide/polyglycolide microparticles)." (p. 14, lines 15-30). These components are the same as those Applicants used and have defined as microcarriers (see specification at p. 6. lines 6-9 and p. 9, lines 7-11).

Applicants have asserted that Carson describes administration of an immunostimulatory polynucleotide conjugated to an antigen. Carson mentions that a colloidal dispersion system may be used to administer the immunostimulatory polynucleotide, however Carson does not describe a complex in which an IMP is linked to the surface of a microcarrier, much less a complex in which an IMP is linked to the surface of a biodegradable microcarrier.

However, Carson does disclose that the microcarrier (i.e. adjuvant, emulsion as defined by Applicants' specification) is conjugated to the ISS (see abstract and p. 3; p. 5).

Applicants have asserted that WO 99/11275 describes administration of an immunostimulatory polynucleotide without co-delivery of an immunizing antigen. WO 99/11275 mentions that a colloidal dispersion system may be used to administer the immunostimulatory polynucleotide, however, WO 99/11275 does not describe a complex in which an IMP is linked to the surface of a microcarrier, much less a complex in which an IMP is linked to the surface of a biodegradable microcarrier.

However, WO 99/11275 discloses that the "...ISS-ODN may be administered with other anti-inflammatory or immunotherapeutic agents. Thus, a particularly useful composition for use in practicing the method of the invention is one in which an anti-inflammatory agent (e.g., a glucocorticoid) or immuno-therapeutic agent (e.g., an antigen, cytokine or adjuvant) is mixed with, or conjugated to, an ISS-ODN." (p. 4, lines 18-22; see also p. 19).

It would appear that the prior art references disclose the claimed invention. Even though the art does not specifically state that the IMP is linked to the surface

of the microcarrier, this is inherent since the components and procedures are the same in the prior art references and the claimed invention and specification.

8. Claims 1-23 and 48-84 are rejected under 35 U.S.C. 102(e) as being anticipated by Friede et al (6544518).

Friede et al disclose a composition comprising CpG, an adjuvant and an antigen (abstract; col. 17). Friede et al disclose that the "...CpG used in the adjuvant combinations of the present invention may be in free solutions or may be complexed to particulate carriers such as mineral salts (for example but not restricted to aluminum or calcium salts), liposomes, ISCOMs, emulsions (oil in water, water in oil, water in oil in water)..." (see col. 4 lines 7-18; col. 4, lines 39-53; col. 5; col. 9). It is noted that claims 48-84 are directed to a kit. The components of the kit are the same as the components of claims 1-23 and it would appear that Schwartz et al would disclose the claimed kit. . Determining the size of the microparticle would have been within the knowledge of a skilled since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

Since the Patent Office does not have the facilities for examining and comparing applicants' complex and kit with the complex and kit of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed complex and kit and the complex and kit of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

The rejection of claims 1-23 and 48-84 under 35 U.S.C. § 102(b) as anticipated by Friede et al 6544518 is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 1-23 and 48-84 under this statutory provision, as set forth in the last Office action. Applicants' arguments filed April 8, 2004, have been fully considered but they are not deemed to be persuasive.

Applicants have asserted that Friede does not describe a complex in which an IMP is linked to the surface of a microcarrier, much less a complex in which an IMP is linked to the surface of a biodegradable microcarrier.

However, as set forth above Friede et al disclose a composition comprising CpG, an adjuvant and an antigen (abstract; col. 17). Friede et al disclose that the "...CpG used in the adjuvant combinations of the present invention may be in free solutions or may be complexed to particulate carriers such as mineral salts (for example but not restricted to aluminum or calcium salts), liposomes, ISCOMs, emulsions (oil in water, water in oil, water in oil in water)..." (see col. 4 lines 7-18; col. 4, lines 39-53; col. 5; col. 9). It would appear that the prior art references disclose the claimed invention. Even though the art does not specifically state that the IMP is linked to the surface of the microcarrier, this is inherent since the components and procedures are the same in the prior art references and the claimed invention and specification.

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N M Minnifield
Primary Examiner
Art Unit 1645

NMM
July 1, 2004